Carbohydrates are the major recognition molecules in many cell-cell interaction events in nature.

Carbohydrates- Chapter 10

- Introduction and definition monosaccharides
- Aldoses and Ketoses
- Cyclic glycosyl residues, Haworth Projections
- Modified monosaccharides
- Glycosidic bond
- Disaccharides
- Polysaccharides
- Peptidoglycans
- Proteoglycans
- Glycoproteins

Carbohydrates

* __________ organic molecule on earth
* __________ (or yield these upon hydrolysis)
* __________: energy storage (glycogen, starch)
  metabolic intermediates (ATP, coenzymes)
  part of DNA & RNA
  structural elements in cell walls of bacteria, fungi & plants
  exoskeleton of arthropods
  extracellular matrix of animals
  cell-cell communication/signalling

• Individual monomeric units are called
  __________________ (CH₂O)n where n≥3
• ____________ (contain 2-20 monosaccharides)
• ____________ (two linked monosaccharides)
• ____________ (> 20 monosaccharides)
• pure mono- & disaccharides are water-soluble, colorless in solution & sweet
• __________________: aldoses & ketoses
_______: carbohydrate polymer

_______: carbohydrate derivative where carbohydrate(s) are linked to a peptide, protein or lipid (i.e. proteoglycans, peptidoglycans, glycoproteins, glycolipids)

_______: study of role of glycans and glycoconjugates in living organisms

_______: compounds with the same molecular formula but different spatial arrangement of their atoms

D & L sugars differ only in steric arrangement of atoms about central C. They are non-superimposable mirror images (i.e. ___________)

They differ in orientation of the crystals, in directions in which solutions rotate polarized light, and in selectivity of reaction with other asymmetric molecules

Fischer projections of: (a) L- and D-glyceraldehyde, (b) dihydroxyacetone

Stereo view of L- and D-glyceraldehyde

See pg. 158
<table>
<thead>
<tr>
<th>N (# of Cs)</th>
<th>Name</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>triose</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>tetrose</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>pentose</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>hexose</td>
<td></td>
</tr>
</tbody>
</table>

For sugars with >1 asymmetric (chiral) carbon, D & L refer to chiral C furthest from aldehyde (or ketone) & correspond to D & L glyceraldehyde

# of stereoisomers = 2^n where n = # of chiral C’s

_____________ : stereoisomers that differ in configuration at only one chiral center

---

**Carbohydrates - Chapter 10**

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- **Aldoses and Ketoses**
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---

**Structure of the 3-6 carbon D-aldoses**

(Blue are the most common)

You must memorize the structures of all the sugars in blue!

(aldoses continued)
Fisher projections of the 3 to 6 carbon D-ketoses (blue structures are most common)

\[
\begin{align*}
\text{Ketone} & \quad \text{CH}_2\text{OH} \\
\text{C} & \quad \text{O} \\
\text{H} - \text{C} - \text{OH} \\
\text{H} - \text{C} - \text{OH} \\
\text{CH}_2\text{OH} \\
\text{D-Ribulose} \\
\text{D-Xylulose} \\
\end{align*}
\]

Dihydroxyacetone

\[
\begin{align*}
\text{Ketone} & \quad \text{CH}_2\text{OH} \\
\text{C} & \quad \text{O} \\
\text{H} - \text{C} - \text{OH} \\
\text{CH}_2\text{OH} \\
\text{D-Erythrose} \\
\end{align*}
\]

\[
\begin{align*}
\text{Ketone} & \quad \text{CH}_2\text{OH} \\
\text{C} & \quad \text{O} \\
\text{H} - \text{C} - \text{OH} \\
\text{H} - \text{C} - \text{OH} \\
\text{H} - \text{C} - \text{OH} \\
\text{H} - \text{C} - \text{OH} \\
\text{H} - \text{C} - \text{OH} \\
\text{D-Talose} \\
\end{align*}
\]

\[
\begin{align*}
\text{Ketone} & \quad \text{CH}_2\text{OH} \\
\text{C} & \quad \text{O} \\
\text{H} - \text{C} - \text{OH} \\
\text{H} - \text{C} - \text{OH} \\
\text{H} - \text{C} - \text{OH} \\
\text{H} - \text{C} - \text{OH} \\
\text{H} - \text{C} - \text{OH} \\
\text{D-Talose} \\
\end{align*}
\]

\[
\begin{align*}
\text{Ketone} & \quad \text{CH}_2\text{OH} \\
\text{C} & \quad \text{O} \\
\text{H} - \text{C} - \text{OH} \\
\text{H} - \text{C} - \text{OH} \\
\text{H} - \text{C} - \text{OH} \\
\text{H} - \text{C} - \text{OH} \\
\text{H} - \text{C} - \text{OH} \\
\text{D-Talose} \\
\end{align*}
\]
Cyclization of Aldoses and Ketoses

Reaction of an alcohol with:
(a) An aldehyde to form a hemiacetal
(b) A ketone to form a hemiketal

See pg. 159-160

(a) Pyran and (b) Furan ring systems

(a) Six-membered sugar ring is a
(b) Five-membered sugar ring is a

See pg. 159-160

Carbohydrates- Chapter 10

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• Glycoproteins
(cyclization of D-glucose, continued)

Haworth Projection

- Reaction of C-5 hydroxyl with one side of C-1 gives α, reaction with the other side gives β

* anomeric carbon
* α and β refer to the anomeric configurations

See Fig. 10.3

Fig. 10.4

Aldoses where Cn (n ≥ 5) or ketoses (n ≥ 6) yield cyclic hemiacetals (or hemiketals) in solution

6 member ring = ___________
5 member ring = ___________

_________ C = most oxidized C of cyclic monosaccharide. It is chiral (i.e. α or β) = anomeric configuration

*** In solution the ring & linear form of monosaccharides are in equilibrium!
Example: D-glucose at 31°C
64% β-D-pyranose
36% α-D-pyranose
< 1% furanose or linear
Cyclization of D-ribose to form α- and β-D-ribopyranose and α- and β-D-ribofuranose

Continued on next slide

31°C at equilibrium

<1% open chain
Conformations of β-D-glucopyranose

Axial substituent: perpendicular to plane of ring

Equatorial substituent: parallel to plane of ring

2 possible conformations (generally more stable)

6 possible conformations

Top conformer is more stable because it has the bulky hydroxyl substituents in equatorial positions (less steric strain)

Carbohydrates - Chapter 8

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Derivatives of Monosaccharides

• Many sugar derivatives are found in biological systems
• Some are part of monosaccharides, oligosaccharides or polysaccharides
• These include sugar phosphates, deoxy and amino sugars, sugar alcohols and acids
Be sure to know these abbreviations

<table>
<thead>
<tr>
<th>Monosaccharide or derivative</th>
<th>Abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhamose</td>
<td>Rib</td>
</tr>
<tr>
<td>Xylose</td>
<td>Xyl</td>
</tr>
<tr>
<td>Hexose</td>
<td>Hex</td>
</tr>
<tr>
<td>Fructose</td>
<td>Fru</td>
</tr>
<tr>
<td>Glucose</td>
<td>Glc</td>
</tr>
<tr>
<td>Manose</td>
<td>Man</td>
</tr>
<tr>
<td>Glucuronic acid</td>
<td>GlcA</td>
</tr>
<tr>
<td>Galacturonic acid</td>
<td>GalUA</td>
</tr>
<tr>
<td>Mannuronic acid</td>
<td>ManA</td>
</tr>
<tr>
<td>Deoxy sugars</td>
<td>Deoxy</td>
</tr>
<tr>
<td>Abequose</td>
<td>Abe</td>
</tr>
<tr>
<td>Fucose</td>
<td>Fuc</td>
</tr>
<tr>
<td>Amino sugars</td>
<td>OGN</td>
</tr>
<tr>
<td>Galactosamine</td>
<td>GalNAc</td>
</tr>
<tr>
<td>N-Acetylgalactosamine</td>
<td>GalNAc</td>
</tr>
<tr>
<td>N-Acetylglucosamine</td>
<td>GaNAc</td>
</tr>
<tr>
<td>N-Acetylmuramic acid</td>
<td>MurNAc</td>
</tr>
<tr>
<td>Sugar phosphates</td>
<td>GLP, GPA, DMP</td>
</tr>
</tbody>
</table>

Some important sugar phosphates

- In deoxy sugars an H replaces an OH

Deoxy sugars

- β-2-Deoxy-β-ribose
- α-L-Fucose
• An amino group replaces a monosaccharide OH
• Amino group is sometimes acetylated
• Amino sugars of glucose and galactose occur commonly in glycoconjugates

(continued)

Sialic acids (e.g. neuraminic acid) are important in animal glycoproteins (formed from ManNAC + pyruvate)

Several _____

• Amino and acetylamino groups are shown in red

\[
\begin{align*}
&\text{N-Acetyl-\(\alpha\)-D-glucosamine} \\
&\text{N-Acetyl-\(\alpha\)-D-galactosamine}
\end{align*}
\]

(continued)

(polyhydroxy alcohols)

• Sugar alcohols: carbonyl oxygen is reduced

Several sugar alcohols

\[
\begin{align*}
&\text{Glycerol} \\
&\text{Myo-inositol} \\
&\text{D-Ribitol}
\end{align*}
\]
• Sugar acids are carboxylic acids
• Produced from aldoses by:
  (1) Oxidation of C-1 to yield an aldonic acid
  (2) Oxidation of the highest-numbered carbon to an alduronic acid

Sugar acids derived from glucose
(example of an aldonic acid)

A lactone is a cyclic ester in organic chemistry. It is the condensation product of an alcohol group and a carboxylic acid group in the same molecules.

(continued)
(example of an alduronic acid)

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**Disaccharides and Other Glycosides**

- __________ - primary structural linkage in all polymers of monosaccharides
- __________ - glucose provides the anomeric carbon
- __________ - a general term meaning that a carbohydrate provides the anomeric carbon

**Glucopyranose + methanol yields a glycoside**

\[
\begin{align*}
\text{Glucopyranose} & \quad + \quad \text{methanol} \\
\xrightarrow{\text{Addition}} & \quad \text{Methyl-α-D-glucopyranoside}
\end{align*}
\]

Under acidic conditions alcohols, amines or thiols can condense with the anomeric C to form a glycosidic bond

**Carbohydrates- Chapter 8**

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**Structures of Disaccharides**

Structures of (a) maltose, (b) cellobiose

\[
\begin{align*}
\text{β-maltose} & \quad \text{β-cellobiose} \\
\text{is a hydrolysis product of amylose (starch)} & \quad \text{is a degradation product of cellulose}
\end{align*}
\]

see Fig. 10.10
Structures of Disaccharides (continued)

Structures of (c) lactose, (d) sucrose

(c) lactose

(d) sucrose

is an abundant disaccharide in milk

: table sugar, most abundant disaccharide in nature, synthesized only in plants

Reducing and Nonreducing Sugars

• Carbohydrates with a reactive carbonyl (i.e. aldoses with free C1) are called reducing because they can reduce metal ions (e.g. Cu$^{2+}$, Ag$^+$)

• Carbohydrates with no free anomeric Carbon are called nonreducing (e.g. sucrose)

See Pg. 161

Nucleosides and Other Glycosides

• Anomeric carbons of sugars can form glycosidic linkages with alcohols, amines and thiols

• : nonsugar molecule attached to the anomeric sugar carbon

• : compound containing glycosidic bonds

• + =

Structures of three glycosides

nucleoside

flavor
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Polysaccharides

• _________ - homopolysaccharides containing only one type of monosaccharide
• _________ - heteropolysaccharides containing residues of more than one type of monosaccharide
• Lengths and compositions of a polysaccharide may vary within a population of these molecules

Starch and Glycogen

• D-Glucose is stored intracellularly in polymeric forms
• Plants and fungi - starch
• Animals - glycogen
• Starch is a mixture of amylose (unbranched) and amylopectin (branched)

Structure of amylose

(a) Amylose is a linear polymer of D-glucose in an α-1,4-linkage; DP of 100-1000
(b) Assumes a left-handed helical conformation in water

DP: degree of polymerization

See Fig. 10.12
**Structure of amylopectin**

Amylopectin is amylose strands connected by an α-1,6-linkage; DP of 300-6000. See Fig. 10.7 & Fig. 10.14

**Comparison of between amylopectic and glycogen**

- Both are energy storage forms of glucose
- Both are strands of α-1,4-linked glucose connected by α-1,6-linkages
- **Amylopectin**: found in plants; DP 300-6000, crystallin, α-1,6-linkages branches occur 1/25 residues
- **Glycogen**: found in animals; DP ≤ 50,000, NOT crystallin, α-1,6-linkages branches occur 1/8 to 1/12 residues

**Cellulose**: most abundant organic molecule on earth, DP 300 - >15,000, synthesized by plants & some bacteria, cell wall polysaccharide

Structure of cellulose (β-1,4-linked glucose homopolymer)

- (a) Chair conformation
- (b) Haworth projection

See Fig. 10.14

**Action of α- and β-amylase on amylopectin (both cleave α-1,4-glucan)**

- **α-amylase** cleaves random internal α-(1-4) glucosidic bonds (endoglycanase)
- **β-amylase** acts on nonreducing ends, exoglycosidase, releases dimers
Stereo view of cellulose fibrils
Individual cellulose chains interact to give cellulose microfibrils and bundles
• Intra- and interchain H-bonding gives strength

In plants a cellulose synthase rosette complex of 6 x 6 cellulose synthase subunits synthesizes a cellulose microfibril of 36 individual cellulose molecules bound together by H-bonds.

Cellulose chains interact via H-bonds to form microfibrils and fibers.

Doblin et al., 2002, Plant Cell Physiol. 43:1407
Structure of chitin: exoskeleton of spiders & crustaceans, & in cell wall of some fungi & algae

- Repeating units of β-(1-4)GlcNAc residues

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Peptidoglycans

- Peptidoglycans - heteroglycan chains linked to peptides
- Major component of bacterial cell walls
- Heteroglycan composed of alternating GlcNAc and N-acetylmuramic acid (MurNAc)
- β-(1 → 4) linkages connect the units


Gram positive bacterium, *Staphylococcus aureus*

Gram-negative bacterium *Escherichia coli*

Glycan moiety of peptidoglycan

MurNAc found only in bacteria and consists of GlcNAc connected at C-3 by an ether linkage to lactate.

Fig. 8.16 A schematic representation of the peptidoglycan in *Staphylococcus aureus*.

Yellow: polysaccharide

Red: tetrapeptide

Blue: pentaglycine

Structure of the peptidoglycan of *Staphylococcus aureus* (gram positive bacteria cell wall peptidoglycan)

(a) Repeating disaccharide unit, (b) Cross-linking of the peptidoglycan macromolecule

Review section pgs. 132-134, Chapter 8
Fig. 8.31 (continued)
(transaccharide, previous slide)

What was the 1st antibiotic discovered?

Penicillin inhibits a transpeptidase involved in bacterial cell wall formation

- Structures of penicillin and -D-Ala-D-Ala
- Penicillin structure resembling -D-Ala-D-Ala is shown in red

Penicillin inhibits a transpeptidase involved in bacterial cell wall formation

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- Lipo-oligosaccharides
- Glycoproteins

Proteoglycans
- _______________ – glycosaminoglycan (~95%)-carbohydrate-protein conjugates. Often found in ECM. Function as lubricants, cell-cell adhesion, messengers, & give tensile strength & elasticity to soft tissues
- _______________ (GAGs) - unbranched heteroglycans of repeating disaccharides (many sulfated hydroxyl and amino groups)
- Disaccharide components include: (1) amino sugar (D-galactosamine or D-glucosamine), (2) an alduronic acid
**Types of GAGs**

1. Not covalently attached to protein  
   *Hyaluronic acid*

2. Covalently attached to proteins (i.e. present in proteoglycans)  
   *Heparin (and heparan sulfate)*  
   *Keratan sulfate*  
   *Chondroitin sulfate*  
   *Dermatan sulfate*

**Proteoglycan aggregate in cartilage**  
~150 GAGs:protein

- Proteoglycans (core proteins with glycosaminoglycan chains attached)  
- Chondroitin sulfate  
- Keratan sulfate  
- Heparin  
- Heparan sulfate

**Repeating disaccharide of hyaluronic acid**

- GlcUA = D-glucuronate
- GlcNAc = N-acetylglucosamine

Hyaluronic acid is GAG not attached to protein
Lipo-oligosaccharides and oligosaccharides can serve as signal molecules

Specific lipo-oligosaccharides are produced by nitrogen-fixing bacteria that interact specifically with certain plants (i.e., legumes) to form root nodules. These lipo-oligosaccharides resemble chitin oligomers with specific modifications.

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Glycoproteins

- Proteins that contain covalently-bound oligosaccharides
- O-Glycosidic and N-glycosidic linkages
- Oligosaccharide chains exhibit great variability in sugar sequence and composition
- ________________ - proteins with identical amino acid sequences but different oligosaccharide chain composition

Four subclasses of ______________ linkages

1. GalNAc-Ser/Thr (most common)
2. 5-Hydroxylysine (Hyl) to D-galactose (unique to collagen)
4. GlcNAc to a single serine or threonine
O-Glycosidic and N-glycosidic linkages

Consensus sequence for N-glycosylation: Asn-X-Ser/Thr

(a) CH₂OH
(b) CH₂OH

Four subclasses of O-glycosidic linkages

(a) NeuAc α(2 → 3) GalNAc β(1 → 3)
(b) Gal — Hyd
(c) Gal — Gal — Xyl — Ser
(d) GlcNAc — Ser/Thr

Structures of N-linked oligosaccharides

(a) Manα(1 → 2)Manα(1 → 2) Manβ(1 → 3)
Manα(1 → 2) Manα(1 → 2) Manβ(1 → 3)
Manα(1 → 2) Manα(1 → 2) Manβ(1 → 3)
Manα(1 → 2) Manα(1 → 2) Manβ(1 → 3)

(b) SAα(2 → 6) Galβ(1 → 4) GlcNAcβ(1 → 2)
SAα(2 → 6) Galβ(1 → 4) GlcNAcβ(1 → 2)
SAα(2 → 6) Galβ(1 → 4) GlcNAcβ(1 → 2)
SAα(2 → 6) Galβ(1 → 4) GlcNAcβ(1 → 2)

(continued)

The oligosaccharides attached to proteins may alter physical properties such as size, shape, solubility, or stability, may effect folding, and/or may have biological roles.

see Fig. 10.15
see Fig. 10.23
see Fig. 10.16
Why do blood transfusions sometimes cause death?
Reason discovered by Karl Landsteiner at University of Vienna in 1901.

All humans and many primates have **A, B, AB or O types** of oligosaccharides on the N-linked and O-linked oligosaccharides on the surface of their red blood cells (includes glycoproteins and glycolipids).

*see Fig. 10.24*